REMARKS

I. Status of the Application

Claims 1-8, 10-15 and 37-56 are presently pending in the application. Claims 1-8, 10-15 37-39 and 40-56 stand rejected as anticipated by, or in the alternative as being unpatentable, over Lam (5,650,489). Claims 1-8, 10-15, 37-39, and 40-56 stand rejected as being unpatentable over Lam (5,650,489) in view of Holmes (5,679,773). Claims 40-48, 50, and 52-56 stand rejected under 35 U.S.C. 112, first paragraph. Applicants respectfully request reconsideration of the application and allowance of the claims.

II. Claims 1-8, 10-15, 37-39 and 40-56 Are Patentable Over Lam

Claims 1-8, 10-15, 37-39 and 40-56 are rejected under 102(e), or in the alternative under 103(a) as obvious, over Lam for the reasons set forth in a previous office action mailed on October 05, 2001. Applicants respectfully traverse the rejection.

Notwithstanding the fact that Lam fails to disclose, teach or suggest synthesis of preselected arrays (as discussed below and demonstrated in previous Responses), Lam fails to disclose, teach or suggest measuring presence of diverse unbound polymers as an indicator of the efficiency of the synthesizing step. The Examiner only cites to Example 7 of Lam disclosed at Column 34, lines 60 to Column 35, lines 55 of Lam.

The Examiner fails to appreciate that no diverse polymers are measured as an indicator of the efficiency of the synthesizing step. Instead, Lam first makes a random peptide according to Example 6. Lam then makes a random peptide using standard solid phase peptide synthesis (SPPS). The different methodologies are then compared to demonstrate that the method of Lam

is superior to the SPPS technique.

Lam, however, fails to disclose, teach or suggest measuring anything as an indicator of efficiency of the synthesizing step. Instead, Lam is comparing the products resulting from performance of all steps of an entire method. In Example 7, Lam's conclusion, after comparison to the SPPS method, is that his method does permit the random synthesis of peptides. Therefore, Lam has not synthesized preselected arrays and measured the presence of diverse unbound polymers as an indicator of the efficiency of the synthesizing step.

The sequencing methods disclosed by Lam neither relate to efficiency nor do they relate to measuring presence of diverse unbound polymers as an indicator of the efficiency of the synthesizing step. Further, Lam fails to even discuss efficiency as an indicator of the synthesizing step. The only discussion of efficiency by Lam relates to the one bead-one peptide synthesis, which as discussed above is not a preselected array. Lam states at Column 11, lines 17-19 that "The one bead-one peptide synthesis allows increased sensitivity and efficiency of isolating the peptide that is specific for the entity to which it binds." At Column 39, lines 49-67, and also in Section 10.3 of Lam, Lam sequenced random peptides in which each bead contained a single species of peptide by sequentially removing a single amino acid at a time using Edman degradation.

It is well known that Edman degradation uses phenylisothiocyanate (Edman's reagent) to react with N-terminal amino acids. The N-terminal amino acid is removed from the protein and forms a thiazolinone derivative with the phenylisothiocyanate. The thiazolinone derivative is placed into aqueous weak acid to form a phenylthiohydantoin (PTH) derivative, which is not a diverse unbound polymer but is instead an amino acid (monomer) derivative. **It is the PTH**

derivative that is measured by the automated sequencer used in Lam and not any unbound polymer as claimed.

Even assuming *arguendo* that Lam does attempt to determine efficiency of a synthesizing step, the PTH derivatives measured by Lam are not diverse unbound polymers of the present invention. **That is, the coupling efficiency of the solid phase peptide synthesis of Lam was performed by measuring single monomer derivatives and not by measuring diverse unbound polymers.** Therefore, the sequencing methods employed by Lam cannot measure the presence of diverse unbound polymers as an indicator of efficiency of the synthesizing step. Accordingly, Lam fails to anticipate or render obvious claims 1-8, 10-15, 37-39 and 40-56.

Applicants filed a Response to the Office Action on January 29, 2002 arguing that Lam failed to teach the subject matter of claims 1-8, 10-15, and 37-39. Applicants believe those arguments still distinguish the claims of the present invention over Lam and hereby incorporate those arguments by reference in this response.

In addition, the arguments in the Response to Office Action mailed on January 29, 2002 are equally applicable to claims 40-56. That is, Lam does not teach or suggest a method of monitoring polymer array synthesis on a solid substrate comprising: (i) synthesizing a preselected array of diverse polymers connected to cleavable linkers on a solid substrate, whereby the diverse polymers occupy different regions of the solid substrate; (ii) cleaving diverse polymers from the solid substrate by cleaving the cleavable linkers, thereby creating a mixture of diverse unbound polymers; and (iii) measuring presence of diverse unbound polymers as an indicator of the efficiency of the synthesizing step, as recited in claim 40. Nor does Lam teach or suggest a method for measuring the effect of altering a polymer array synthesis protocol,

comprising: (i) synthesizing a preselected array of diverse polymers occupying different regions on a solid support by a first synthesis protocol, thereby creating a reference array of polymers; (ii) synthesizing a preselected array of diverse polymers occupying different regions on a solid support synthesized by a second synthesis protocol, wherein the second synthesis protocol is different than the first synthesis protocol, thereby creating a test array of polymers; (iii) cleaving separately the reference array of polymers and the test array of polymers, thereby creating a mixture of diverse cleaved polymers from the reference array and a mixture of diverse cleaved polymers from the test array; (iv) measuring presence of diverse cleaved polymers from the test array as an indicator of the efficiency of the first synthesis procedure and measuring presence of the mixture of diverse cleaved polymers from the reference array as an indicator of the efficiency of the second synthesis procedure, thereby determining whether a difference between the first and second synthesis procedures affects the efficiency of the second synthesis procedure, as recited in claim 50. Instead, Lam only discloses single bead-single polymer libraries that are random, and Lam does not disclose synthesizing preselected arrays of diverse polymers. Accordingly, claims 1 and 50 are patentable over Lam. Claims 41-49 depend directly or indirectly from claim 40 and are patentable for at least the same reasons. Claims 51-56 depend directly or indirectly from claim 50 and are patentable for at least the same reasons.

At least, the Examiner acknowledges in paragraph number 13 of the Office Action that preparation of preselected arrays, e.g. spatially addressable libraries on supports, is not a preferred embodiment set forth in Lam. Applicants respectfully submit that Lam fails to teach preselected arrays whether as a preferred embodiment or not. The Examiner, however, asserts that it is an immediately envisioned embodiment in view of the disclosure of Lam. Applicants

disagree and submit that the Examiner is using impermissible hindsight reconstruction based on the applicants' own disclosure. Such practice is plainly not allowed.

The Examiner has provided no objective evidence that one skilled in the art would immediately envision preselected arrays in view of Lam. In the absence of objective evidence demonstrating some suggestion or motivation that those skilled in the art would modify Lam to arrive at preselected arrays, no *prima facie* cause of obviousness has been established. Accordingly, claims 1-8, 10-15, 37-39 and 40-56 are not obvious over Lam.

Therefore, for the reasons stated above Lam does not anticipate claims 1-8, 10-15, 37-39 and 40-56 and claims 1-8, 10-15, 37-39 and 40-56 are not obvious over Lam. Applicants believe the rejection to be improper and request withdrawal of the rejection and allowance of claims 1-8, 10-15, 37-39 and 40-56.

III. Claims 1-8, 10-15, 37-39 and 40-56 are Patentable Over Lam in view of Holmes

Claims 1-8, 10-15, 37-39 and 40-56 are rejected under 103(a) as obvious over Lam in view of Holmes for the reasons set forth in a previous office action mailed on October 05, 2001. Applicants respectfully traverse the rejection.

Lam in view of Holmes does not render claims 1-8, 10-15, 37-39 and 40-56 obvious because (i) Lam in view of Holmes fails to teach or suggest all elements of the claims, and (ii) there is no reasonable expectation of success of arriving at Applicants' claimed subject matter because the teachings of Lam and Holmes are in conflict and, therefore, are not properly combinable. In addition, the combination of Lam and Holmes would render Lam unsatisfactory for its intended purpose and would unavoidably alter the principle operation of Lam.

a. The Combination of Lam and Holmes fails to Teach or Suggest All Elements of Claims 1-8, 10-15, 37-39 and 40-56

It is well accepted that one of the three requirements necessary to establish a *prima facie* case of obviousness is that the combination of citations must teach or suggest all claim elements. *In re Vaeck.* 947 F.2d 488, 20 USPQ 2d 1438 (Fed. Cir. 1991). As discussed below, because the combination of Lam and Holmes fails to teach or suggest all claim elements, claims 1-8, 10-15, 37-39 and 40-56 are patentable over Lam in view of Holmes.

The combination of Lam and Holmes fails to teach or suggest a preselected array. Lam only teaches random peptides, as discussed above, and Holmes only teaches synthesis using preselected monomers at a predefined region (See Col. 6, lines 46-65 and Col. 7, lines 25-30). Accordingly, the combination of Lam and Holmes fails to teach the first element of claim 1, the first element of claim 40 and the first two elements of claim 50. Therefore, each of claims 1, 40 and 50 are patentable over the combination of Lam and Holmes because the combination clearly fails to teach or suggest all the elements of claim 1, claim 40 and claim 50.

Claims 2-8, 10-15 and 37-39 depend directly or indirectly from claim 1, claims 41-49 depend directly or indirectly from claim 40, and claims 51-56 depend directly or indirectly from claim 50. Accordingly, claims 2-8, 10-15, 37-39, 41-49 and 51-56 are patentable over the combination of Lam and Holmes for at least the same reasons. Applicants believe the rejection to be improper and request withdrawal of the rejection and allowance of the claims.

The combination of Lam and Holmes fails to teach or suggest measuring the presence of diverse unbound polymers as an indicator of the efficiency of the synthesizing step, as recited in claims 1 and 40. The combination of Lam and Holmes also fails to teach or

suggest measuring presence of diverse cleaved polymers from the test array as an indicator of the efficiency of the first synthesis procedure and measuring presence of the mixture of diverse cleaved polymers from the reference array as an indicator of the efficiency of the second synthesis procedure, thereby determining whether a difference between the first and second synthesis procedures affects the efficiency of the second synthesis procedure, as recited in claim 50.

As discussed above, Lam does not teach or suggest any step of measuring presence of diverse unbound polymers as an indicator of the synthesizing step, but instead, Lam teaches away by measuring monomeric derivatives, i.e. unbound monomers such as PTH derivatives from Edman degradation. Holmes cannot cure this teaching of Lam, because Holmes teaches measurement of fidelity of synthesis which occurs on a solid substrate, and comparison with known standards to provide a confirmation of synthesis fidelity (See Column 19, lines 34-55 of Holmes). Applicants believe the rejection to be improper and request withdrawal of the rejection and allowance of the claims.

Further, the Examiner is required to consider the claims as a whole rather than merely selecting one or more elements from the claims and piecewise assembling citations which only teach or suggest individual elements of the claims. It is well established that in determining the differences between the prior art and the claims, the question under 35 U.S.C. 103 is not whether the differences themselves would have been obvious, but whether the claimed invention as a whole would have been obvious. See *Stratoflex Inc. v. Aeroquip Corp.*, 713 F.2d 1530, 218 USPQ 871 (Fed. Cir. 1983).

When considering the method of each of claims 1 and 40 as a whole, the combination of Lam and Holmes fails to teach or suggest any method which involves synthesizing a preselected array of diverse polymers, cleaving the diverse polymers from a substrate and measuring presence of diverse unbound polymers as an indicator of the efficiency of the synthesizing step. Accordingly, claims 1 and 40 are patentable over the combination of Lam and Holmes. Because claims 2-8, 10-15 and 37-39 depend directly or indirectly from claim 1, and claims 41-49 depend directly or indirectly from claim 40, these claims are patentable over the combination of Lam and Holmes for at least the same reasons.

When considering the method of claim 50 as a whole the combination of Lam and Holmes fails to teach or suggest any method of synthesizing a preselected array of diverse polymers occupying different regions on a solid support by a first synthesis protocol, synthesizing a preselected array of diverse polymers occupying different regions on a solid support synthesized by a second synthesis protocol, wherein the second synthesis protocol is different than the first synthesis protocol, thereby creating a test array of polymers, and cleaving each of the preselected arrays of polymers and measuring presence of diverse cleaved polymers from the test array as an indicator of the efficiency of the first synthesis procedure and measuring presence of the mixture of diverse cleaved polymers from the reference array as an indicator of the efficiency of the second synthesis procedure, thereby determining whether a difference between the first and second synthesis procedures affects the efficiency of the second synthesis procedure. Accordingly, claim 50 is patentable over the combination of Lam and Holmes. Because claims 51-56 depend directly or indirectly from claim 50, these claims are patentable over the combination of Lam and Holmes for at least the same reasons.

For the reasons above, the combination of Lam and Holmes fails to teach or suggest the subject matter of any of the claims, and, therefore, the rejection of the claims is improper and should be withdrawn. Applicants request withdrawal of the rejection and allowance of each of claims 1-8, 10-15, 37-39 and 40-56.

b. The Combination of the Citations Provides No Reasonable Expectation of Success in Arriving at Applicants' Claimed Subject Matter

It is well accepted that a second requirement to establish a *prima facie* case of obviousness is that there must be some reasonable expectation of success in arriving at Applicants' claimed invention. *In re Vaeck*, 947 F.2d 488, 20 USPQ 2d 1438 (Fed. Cir. 1991). As discussed below, because Lam and Homes cannot be properly combined, Lam and Holmes cannot render the claims *prima facie* obviousness.

1. The Combination of Lam and Holmes would render Lam Unsatisfactory for its Intended Purpose

The combination of Lam and Holmes would render Lam unsatisfactory for its intended purposes. It is well accepted that if proposed modification would render the citation unsatisfactory for its intended purposes, then there is no suggestion or motivation to make the proposed modification. *In re Gordon*, 733 F.2d 900, 221 USPQ 1125 (Fed. Cir. 1984).

As discussed above, an intended purpose of Lam is to evaluate the peptide synthesis by measuring single monomer derivatives and not by measuring diverse unbound polymers. To combine Holmes with Lam would require that Lam not measure monomer derivatives, because Holmes requires measurement of fidelity of synthesis which occurs on a solid substrate, and

comparison with known standards to provide a confirmation of synthesis fidelity. (The single monomer derivatives of Lam cannot be on a solid substrate). Thus, to combine Lam and Holmes would require that Lam not measure monomer derivatives to evaluate synthesis. That is, to combine Lam and Holmes would require that Lam abandon his evaluation methods, which would render Lam unsatisfactory for its intended purpose.

Because the combination of Lam and Holmes would render Lam unsatisfactory for its intended purposes, there is no suggestion to make the modification proposed by the Examiner. Accordingly, Applicants believe the rejection to be improper and request withdrawal of the rejection and allowance of the claims.

2. The combination of Lam and Homes would Unavoidably alter the Principle Operation of Lam

The combination of Lam and Holmes would unavoidably alter the principle operation of Lam. It is well settled that if a proposed modification or combination of the citations would change the principle operation of the citation being modified, then the teachings of the citations are not sufficient to render the claims *prima facie* obvious. *In re Ratti*, 20 F.2d 810, 120 USPQ 349 (CCPA 1959).

As discussed above, the principle operation of Lam is to evaluate the peptide synthesis by measuring single monomer derivatives and not by measuring diverse unbound polymers. To combine Holmes with Lam would require that Lam not measure monomer derivatives, but instead evaluate synthesis using the method of Holmes, which requires measurement of fidelity of synthesis which occurs on a solid substrate, and comparison with known standards to provide a confirmation of synthesis fidelity. Thus, the proposed modification to Lam would unavoidably

alter the principle operation of Lam. That is, to combine Lam and Holmes would require that Lam abandon his evaluation methods, which can only alter the principle operation of Lam.

Accordingly, because the combination of Lam and Holmes would unavoidably alter the principle operation of Lam, the combined teachings of the Lam and Holmes are not sufficient to render the claims *prima facie* obvious. Applicants believe the rejection to be improper and request withdrawal of the rejection and allowance of the claims.

IV. Claims 40-48, 50, and 52-56 meet the Requirements of 35. U.S.C. § 112, first paragraph

At page 3, numbered paragraph 8, claims 40-48, 50 and 52-56 are rejected as containing subject matter which was not described in the specification in such a way to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. At page 5, numbered paragraph 9, claims 40-48, 50 and 52-56 are rejected under 112, first paragraph. The Examiner is of the opinion that the specification, while being enabling for nucleotides, peptides and peptide nucleic acids does not reasonably provide enablement for an array of diverse polymers. Applicants traverse these rejections for the reasons below.

a. Claims 40-48, 50 and 52-56 are Patentable Because the Specification as filed Meets the Written Description Requirement of 35 U.S.C. § 112, first paragraph

Claims 40-48, 50 and 52-56 meet the written description requirement of 35 U.S.C. § 112, first paragraph. Applicants are neither required to disclose nor describe every species to meet the written description requirement. The Examiner is of the opinion that the genus of polymers in claims 40-48, 50 and 52-56 is indefinitely large. The Examiner also believes that the claimed

invention contains no identifying characteristics of polymers prepared by the claimed method. Finally, the Examiner asserts that the narrow scope of the examples directed to specific peptides or nucleic acids is not representative of the scope of the array of compounds. Applicants traverse the rejection.

Claims 48-48, 50 and 52-56 are patentable because the specification as filed meets the written description requirement of 35 U.S.C § 112, first paragraph. To fulfill the written description requirement, a patent specification must only describe an invention in sufficient detail so that one skilled in the art could clearly conclude that the inventor invented the claimed invention. See *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997). That is, adequate written description may be shown by any description of sufficient, relevant and identifying characteristics so long as a person skilled in the art would recognize that the inventor had possession of the claimed invention. See *Purdue Pharma L.P. v. Faulding, Inc.*, 230 F.3d 1320, 1323, 56 USPQ2d 1481, 1483 (Fed. Cir. 2000).

The extensive specification and examples therein provide more than sufficient detail such that one skilled in the art could conclude that the inventor invented the claimed invention. Furthermore, the examples of the specification clearly demonstrate relevant characteristics in synthesizing a preselected array of diverse polymers. For example, numerous descriptions in the specification disclose embodiments where amino acids are used as the monomers to synthesize diverse polymers. Such synthesis occurs through the coupling of amino groups and carboxyl groups, for example. Therefore, any other monomers having amino and carboxyl groups could be coupled similarly by one skilled in the art using routine experimentation. Accordingly, one skilled in the art, in view of the specification, could readily synthesize diverse polymers from

amino acids or could synthesize diverse polymers from other species having amino groups and carboxyl groups.

Even if the synthesis of diverse polymers, or any of the reactions used to perform the synthesis of diverse polymers, were more difficult to synthesize than the diverse polymers disclosed in the specification, or even if synthesis of any diverse polymers required more experimentation than the experimentation required to synthesize the diverse polymers disclosed in the specification, such difficulty or additional experimentation does not mean that the specification is inadequate. That is, just because producing some diverse polymers may be more difficult than producing other diverse polymers, does not mean the specification is inadequate. See *Johns Hopkins Univ. v. Cell Pro, Inc.*, 15 2 F.3d, 1342, 1360-61, 47 USPQ2d 1705, 1718-19 (Fed. Cir. 1998) holding that even though it was more difficult to produce a certain antibody, this difficulty was not attributable to a failure of disclosure in the specification. Accordingly, even if it is more difficult to synthesize some of the species of diverse polymers, the representative examples and description in the specification provide adequate disclosure such that one skilled in the art could synthesize any species of diverse polymers within the scope of claims 40-48, 50 and 52-56. Accordingly, the specification as filed satisfies the written description requirement of 35 U.S.C. § 112, first paragraph.

The Examiner seemingly is requesting that Applicants provide examples that represent every possible species encompassed by the genus of diverse polymers. Such a requirement by the Examiner, however, is inapposite to the Federal Circuit's holdings with respect to adequate disclosure of genera. It is well settled that Applicants need not disclose every species of the present invention. See *Durel Corp. v. Osram Sylvania Inc.*, 52 USPQ2d 1418, 1431 (D. Ariz.,

1998), *rev'd* 256 F.3d 1298, 59 USPQ2d 1238 (Fed. Cir. 2001). That is, the Federal Circuit has held that every species in a genus need not be described in order for a genus to meet the written description requirement. See also *Utter v. Hiraga*, 845 F.2d at 998-99, 6 USPQ 2d at 1714 (Fed. Cir. 1988).

Those skilled in the art in view of the specification as filed, and in view of what is known and what is conventional, have been appraised of the scope of the invention. That is, with respect to the genus of diverse polymers claimed by Applicants in claims 40-48, 50 and 52-56, those skilled in the art, using their knowledge, skill, and conventional methods, have been provided with sufficient detail so that they would clearly conclude that the inventor invented the claimed subject matter of claims 40-48, 50 and 52-56. Accordingly, the specification as filed meets the written description requirement of 35 U.S.C. § 112, first paragraph.

The Examiner inappropriately relies on *Univ. of CA v. Eli Lilly & Co.*, 43 USPQ2d 1398, 1405 (Fed. Cir. 1997), whose holding was narrowly directed towards product claims to cDNA. See *Eli Lilly*, 43 USPQ2d at 1406 where the court suggests normal tests used by the court for written description and enablement were not applicable to the cDNA product claims at issue in *Eli Lilly*. The court fails to state, or even suggest, that the holding of *Eli Lilly* would be applicable to synthesis of diverse polymers. The Examiner refers Applicants to the citation of *Fiers* in *Eli Lilly*. *Fiers* 984 F.2d at 1171, 25 USPQ2d at 1606. However, *Fiers*, which is cited along with *In re Smythe*, 480 F.2d 1376, 178 USPQ 279 (CCPA 1973), requires unpredictability in performance with respect to species that are not disclosed in the specification.

The Examiner has provided no such evidence that the diverse polymers of claims 40-48, 50 and 52-56 are unpredictable such that one skilled in the art, in view of the specification as

filed and in view of knowledge in the art, could not arrive at Applicants' invention. Accordingly, claims 40-48, 50 and 52-56, in view of the adequate specification as filed, meet the written description requirement of 35 U.S.C. § 112, first paragraph.

The court in *Eli Lilly* also held that a definition of function alone does not suffice to describe a coding sequence because it is only an indication of what the gene does, rather than what it is. *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406. In the present invention, the specification clearly states what the diverse polymers are. That is, the diverse polymers in the specification are not defined by what they do, but instead are defined by what they are. Accordingly, the specification as filed meets the written description requirement of 35 U.S.C. § 112, first paragraph.

With respect to the number of species disclosed by Applicants, the Federal Circuit has held that Applicants need only disclose a representative number of species. In fact, the court has held that there are situations where disclosure of a single species adequately supports a genus. See *In re Rasmussen*, 650 F.2d 1212, 1214, 211 USPQ 323, 326-27 (CCPA 1981). What constitutes a representative number of species is an inverse function of the skill and knowledge in the art.

The skill and knowledge in the art of the subject matter of claims 40-48, 50 and 52-56 is extremely high. Accordingly, the number of representative species that need to be disclosed is extremely low. In addition to peptides and nucleic acids, Applicants disclose numerous other species. For example, at page 3, line 27 to page 4, lines 5 of the specification, Applicants state:

> The methods are generally suitable to any polymer array, regardless of the type of polymer. Thus, the efficiency of synthesis for biological polymers such as proteins, nucleic acids, antigens

> and venoms are monitored using the above method. Non-biological polymers such as carbon chains, vinyls, alcohols and other polymers are similarly monitored. The polymer array is typically provided by synthesizing the array on the solid substrate, but the array can also be provided by synthesizing the polymers to be attached to the array in solution, and subsequently attaching the polymers to preselected sites in the array.

Because, of the extremely high level of skill in the art, the specification discloses more than enough species to provide a representative number of species. In addition, such species have been described in sufficient detail so that one skilled in the art could clearly conclude that the inventor invented the claimed invention. Accordingly, the specification as filed meets the written description requirement of 35 U.S.C. § 112, first paragraph.

For the reasons above, the specification as filed meets the written description requirement of 35 U.S.C. § 112, first paragraph and claims 40-48, 50 and 52-56 are patentable. Applicants believe the rejection to be improper and request withdrawal of the rejection and allowance of the claims.

b. Claims 40-48, 50 and 52-56 are Patentable because the Specification as filed meets the Enablement Requirement of 35 U.S.C. § 112, first paragraph

Claims 48-48, 50 and 52-56 are patentable because the specification as filed meets the enablement requirement of 35 U.S.C § 112, first paragraph. The enablement requirement is met if the specification enables any mode of making and using the invention. See *Durel Corp. v. Osram Sylvania, Inc.*, 52 USPQ2d 1418, 1431(D. Ariz., 1998), rev'd 256 F.3d 1298, 59 USPQ2d 1238 (Fed. Cir. 2001) quoting *Johns Hopkins Univ. v. Cell Pro, Inc.*, 152 F.3d 1342, 47 USPQ2d 1705 (Fed. Cir. 1998). The specification as filed discloses numerous modes of making and using the invention which are applicable to diverse polymers within the scope of the claims.

The specification states at page 3, line 27 to page 4, line 1 that:

> The methods are generally suitable to any polymer array, regardless of the type of polymer. Thus, the efficiency of synthesis of biological polymers such as proteins, nucleic acids, antigens, and venoms are monitored using the method above. Non-biological polymers such as carbon chains, vinyl alcohols, and other polymers are similarly monitored.

The specification states on page 19, lines 20-27 that:

> As described above, diverse methods of making polymer arrays are known; accordingly no attempt is made to describe or catalogue all known methods. For exemplary purposes, light directed VLSPIS methods are briefly described below. One of skill will understand that alternate methods of creating polymer arrays, such as spotting and/or flowing reagents over defined regions of a solid substrate, bead based methods and pin-based methods are also known and applicable to the present invention (See, Holmes et al. (filed 17/95) SN 08/374,492).

The specification further states on page 40 that:

> The following examples are provided by way of illustration only and not by way of limitation. One of skill will recognize a variety of parameters which can be changed or modified to yield essentially similar results.

In view of the detailed specification, the examples therein and the related patents and patent applications referenced in the specification, one skilled in the art could make and use diverse polymers within the scope of the claimed invention. Accordingly, the specification meets the enablement requirement of 35 U.S.C. § 112, first paragraph.

The Examiner is of the opinion, however, that the specification is not enabled, because, the Examiner asserts, that Applicants have not provided working examples that are commensurate in scope with the claims. Applicants disagree.

The Examiner fails to realize that illustrative examples are not required to enable a patent application. See *Johns Hopkins Univ. v. Cell Pro, Inc.*, 152 F.3d 1342, 47 USPQ2d 1705 (Fed. Cir. 1998). In *Cell Pro*, the patent claimed a genus of antibodies but only a single antibody had been produced. The Federal Circuit affirmed the district court ruling that the patent was not invalid for want of enablement even though the lab of another inventor failed to produce a second antibody after a major effort. *Cell Pro*, 152 F.3d at 1360, 47 USPQ2d at 1718.

Unlike *Cell Pro*, where only a single embodiment of a genus was disclosed, Applicants have provided numerous embodiments which fall within the genus of diverse polymers. Therefore, if the single embodiment in *Cell Pro* met the enablement requirement, the numerous embodiments of the present invention must certainly meet the enablement requirement. Further, the scope of enablement must only bear a reasonable correlation to the scope of the claims (See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970)). The disclosure of numerous embodiments of diverse polymers taken in conjunction with the specification, the examples therein and the information available in the patents and patent applications cited in the specification, provides information which is at least commensurate with the scope of the claims if not more so.

In addition, just because a large number of diverse polymers could result, does not mean that the specification is not enabled. The Federal Circuit has held that a specification is enabling even though it lists elements that could form thousands of end products. *Atlas Powder Co. v. E.I. duPont de Nemours & Co.*, 750 F.2d 1569, 224 USPQ 409 (Fed. Cir. 1984). Accordingly, in view of *Atlas Powder Co.*, the Examiner's assertion that the claims encompass any polymer, and therefore the enablement requirement is not met, is improper.

Those skilled in the art would not be required to undertake undue experimentation to arrive at Applicants' claimed subject matter. The Examiner has failed to provide any evidence that one skilled in the art would have to undertake undue experimentation to arrive at Applicants' claimed subject matter. Just because the experimentation may be difficult does not make it undue. See *In re Wands*, 858 F.2d 731, 737, 8 USPPQ 2d 1400, 1404 (Fed. Cir. 1988). Experimentation is not undue if those skilled in the art typically engage in such experimentation. *Massachusetts Institute of Technology v. A.B. Fortia*, 774 F.2d 1104, 227 USPQ 428 (Fed. Cir. 1985). Because no such evidence has been provided by the Examiner that undue experimentation would be required by those skilled in the art after viewing the detailed specification, the examples therein, and the patents and patent applications cited therein, the claims meet the enablement requirement of 35 U.S.C. § 112, first paragraph.

In particular, the numerous patents and patent applications cited in the specification provide detailed information of synthesizing diverse polymer sequences. For example, on page 19, line 18 of the instant specification, Applicants refer to U.S.S.N. 07/980,532, filed on Nov. 20, 1992, (now issued as U.S. Patent No. 5,677,195, a copy of which is attached as Exhibit A and referred to below as the '195 patent) that describes combinatorial strategies for polymer synthesis. The Abstract of the '195 patent states that:

> A method and device for forming large arrays of polymers on a substrate (401). According to a preferred aspect of the invention, the substrate is contacted by a channel block (407) having channels (409) therein. Selected reagents are delivered through the channels, the substrate is rotated by a rotating stage (403), and the process is repeated to form arrays of polymers on the substrate. The method may be combined with light-directed methodologies.

At column 1, lines 12-15, the specification of the '195 patent states that:

> The present invention relates to the field of polymer synthesis and screening. More specifically, in one embodiment the invention provides an improved method and system for synthesizing arrays of diverse polymer sequences.

At column 5, lines 14-31, the specification of the '195 patent states that:

> The invention is described herein primarily with regard to the preparation of molecules containing sequences of monomers such as amino acids, but could readily be applied in the preparation of other polymers. Such polymers include, for example, both linear and cyclic polymers of nucleic acids, polysaccharides, phospholipids, and peptides having either alpha.-,.beta.-, or .omega.-amino acids, heteropolymers in which a known drug is covalently bound to any of the above, polynucleotides, polyurethanes, polyesters, polycarbonates, polyureas, polyamides, polyethyleneimines, polyarylene sulfides, polysiloxanes, polyimides, polyacetates, or other polymers which will be apparent upon review of this disclosure. Such polymers are "diverse" when polymers having different monomer sequences are formed at different predefined regions of a substrate. Methods of cyclization and polymer reversal of polymers are disclosed in copending application Ser. No. 796,727, filed Nov. 22, 1991, entitled "POLYMER REVERSAL ON SOLID SURFACES," incorporated herein by reference for all purposes.

The '195 patent goes on to describe numerous embodiments for making and using polymers.

Also on page 19, line 18 of the instant specification, Applicants refer to U.S.S.N. 07/796,243 filed on Nov. 22, 1991 (which issued on Jan, 24, 1995 as U.S. Patent No. 5,384,261, a copy of which is attached as Exhibit B and referred to below as the '261 patent) that describes very large scale immobilized polymer synthesis using mechanically directed flow paths. At column 2, lines 28-40, the '261 patent states that:

> Accordingly, one embodiment of the invention provides a method of forming diverse polymer sequences on a single substrate, the substrate comprising a surface with a plurality of selected regions. The method includes the steps of forming a plurality of channels adjacent the surface, the channels at least partially having a wall

> thereof defined by a portion of the selected regions; and placing selected reagents in the channels to synthesize polymer sequences at the portion of the selected regions, the portion of the selected regions comprising polymers with a sequence of monomers different from polymers in at least one other of the selected regions.

The '261 patent goes on to describe numerous embodiments for making and using diverse polymer sequences.

Further, on page 19, line 14 of the instant specification, Applicants refer to U.S. Patent No. 5,143,854 (which is attached as Exhibit C and referred to below as the '854 patent), issued on Sept. 1, 1992, that describes large scale photolithographic solid phase synthesis of polypeptides and receptor binding screening thereof. At column 1, lines 26-37, the '854 patent states that:

> The present inventions relate to the synthesis and placement of materials at known locations. In particular, one embodiment of the inventions provides a method and associated apparatus for preparing diverse chemical sequences at known locations on a single substrate surface. The inventions may be applied, for example, in the field of preparation of oligomer, peptide, nucleic acid, oligosaccharide, phospholipid, polymer, or drug congener preparation, especially to create sources of chemical diversity for use in screening for biological activity.

Columns 11-16 of the '854 patent describe numerous embodiments for polymer synthesis. The specification states at Column 15, line 64 to Column 16, line 1 that

> In some embodiments a single substrate supports more than about 10 different monomer sequences and preferably more than about 100 different monomer sequences, although in some embodiments more than about 10^3, 10^4, 10^5, 10^6, 10^7, or 10^8 different sequences are provided on a substrate.

The '854 patent goes on to describe numerous embodiments for making and using polymers comprising diverse chemical sequences.

In addition, on page 19, lines 26-27 of the instant specification, Applicants refer to U.S.S.N. 08/374,492, filed on Jan. 17, 1995 (now issued as U.S. Patent No. 5,679,773, a copy of which is attached as Exhibit D and referred to below as the '773 patent), that describes reagents and methods for immobilized polymer synthesis and display. The '773 patent states at Column 1, lines 5-10 that:

> The present invention relates to the field of solid phase polymer synthesis. More specifically, the invention provides methods and reagents for solid phase synthesis of oligomer arrays which may be used, for example, in screening studies for determination of binding affinity.

The '773 patent states at Column 2, lines 1-8 that:

> The present invention provides new compounds, compositions and methods which find application in solid phase synthesis including the preparation of high-density arrays of diverse polymer sequences such as diverse peptides and oligonucleotides as well as in preparation of arrays of small ligand molecules.

The '773 patent goes on to describe numerous embodiments for making and using polymers.

On page 23, line 4 of the instant specification, Applicants refer to U.S.S.N 08/146,886 filed on Nov. 2, 1993 (now issued as U.S. Patent No. 5,639,603, a copy of which is attached as Exhibit E and referred to below as the '603 patent) that describes synthesizing and screening molecular diversity. The '603 patent states at Column 1, lines 12-21 that:

> The present invention relates generally to methods for synthesizing very large collections of diverse molecules and for identifying and isolating compounds with useful and desired activities from such collections. The invention also relates to the incorporation of

> identification tags in such collections to facilitate identification of compounds with desired properties. The invention therefore relates to the fields of chemistry, biology, pharmacology, and related fields.

The '603 patent goes on to describe numerous embodiments for making and using chemical libraries including polymer libraries.

In addition to the patents discussed above, Applicants refer to numerous other patents and patent applications in the specification. For example, on page 19, line 9 of the instant specification, Applicants refer to U.S.S.N. 08/327,687 filed on Oct. 24, 1994 (now issued as U.S. Patent No. 5,556,752, a copy of which is attached as Exhibit F) that describes preparation of libraries of oligonucleotides. On page 23, line 4 of the instant specification, Applicants refer to U.S.S.N. 07/946,239 filed on Sept. 16, 1992 (now issued as U.S. Patent No. 5,770,358, a copy of which is attached as Exhibit G) that describes the preparation of oligomers. On page 23, line 5 of the instant specification, Applicants refer to U.S.S.N. 07/876,792 filed on April 29, 1992 (now issued as U.S. Patent No. 5,541,061, a copy of which is attached as Exhibit H) that describes methods of preparing and screening polymers.

In view of the instant specification, the figures, the examples and the teachings of the numerous patent and patent applications cited in the specification (only some of which are discussed above), one skilled in the art could readily make and use the subject matter within the scope of the claimed invention.

In addition to the patent and patent applications cited in the specification, material outside of the specification can be resorted to in order to satisfy the enablement requirement because it makes no sense to encumber the specification of a patent with all knowledge of the past concerning how to make and use the claimed invention. See *Amtel Corp. v. Information Storage*

Devices, 198 F.3d 1374, 1382, 53 USPQ2d 1225, 1230 (Fed. Cir. 1999). Therefore, because one skilled in the art could readily make and use the claimed invention using knowledge of the past concerning how to make and use the claimed invention and in view of the detailed specification, the examples therein, and the patents and patent applications cited therein, the claimed invention meets the enablement requirement of 35 U.S.C. § 112, first paragraph.

The Examiner asserts that the specification fails to give adequate direction and guidance in the preparation of arrays of polymers commensurate with diverse polymers. Applicants disagree.

The Examiner has failed to consider the numerous patent and patent application referred to in the specification and has also failed to realize that information outside the specification that is known to those skilled in the art can be resorted to in order to satisfy the enablement requirement. In fact, the Federal Circuit has held "what is well-known is best omitted from the specification." See *In re Buchner*, 929 F.2d 660, 661, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991). In view of the specification as filed and in view of information which was available and known to those skilled in the art at the time the invention was made, including the Cho article, for example, those skilled in the art could make and use the claimed invention without undue experimentation.

For the reasons above, the specification as filed meets the enablement requirement of 35 U.S.C. § 112, first paragraph and claims 40-48, 50 and 52-56 are patentable. Applicants believe the rejection to be improper and request withdrawal of the rejection and allowance of the claims.

V. Obviousness Type Double Patenting Rejections

Claims 1-8, 10-15, 37-39 and 40-56 are rejected under the judicially created doctrine of obviousness type double patenting as being unpatentable over claims 2-17 of U.S. Patent No. 5,843,655. Claims 1-8, 10-15, 37-39 and 40-56 are rejected under the judicially created doctrine of obviousness type double patenting as being unpatentable over claims 1-39 of U.S. Patent No. 6,238,862. Applicants traverse the rejection.

Claims 1-8, 10-15, 37-39 and 40-56 are patentably distinct from the U.S. Patent Nos. 5,843,655 and 6,238,862. Just because the claims of the present invention may be directed to solving the same problem as U.S. Patent Nos. 5,843,655 and 6,238,862 does not mean that the claims of the present invention are not patentably distinct.

Notwithstanding this traversal, to advance issuance of the pending claims enclosed herewith is a terminal disclaimer signed by the attorney of record. Applicants request allowance of all claims.

VI. Conclusion

Applicants have also shown that Lam clearly fails to disclose, teach or suggest preselected arrays and/or measuring the presence of diverse unbound polymers. Applicants have also shown that the combination of Lam and Holmes cannot render any of the claims obvious. Further, Applicants have clearly demonstrated that the specification as filed meets the enablement and written description requirements of 35 U.S.C. § 112, first paragraph.

Having addressed all outstanding issues, Applicants respectfully request allowance of the case. To the extent the Examiner believes that it would facilitate allowance of the case, the Examiner is invited to telephone the undersigned at the number below.

Respectfully submitted,

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John P. Iwanicki
Reg. No. 34,628
BANNER & WITCOFF, LTD.
28 State Street, 28th Floor
Boston, MA 02109 (617) 227-7111